REMARKS

Reconsideration of this application, in view of the amendment and the below remarks, is respectfully requested.

The present amendment is made to comply with the Examiner's stipulation that the nonelected subject matter must be canceled in response to the final rejection. It is respectfully requested that the amendment be entered in the record, albeit after a final rejection, since this amendment directly pertains to and satisfies the Examiner's requirement. If the Examiner approves the amendment, the pending claims will be drawn to the elected Group II wherein Y is heteroaryl. Applicants reserve the right to file a divisional application directed to the nonelected subject matter, if desired, in due course.

Claims 1, 2 and 5-7 remain rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement for reasons set forth on pages 2 and 3 of the Office action. Applicants respectfully traverse the rejection in light of the arguments of record (incorporated herein by reference thereto) and the following additional reasons.

Applicants have been researching and discovering novel hydroxamic acid compounds that possess TACE inhibiting activity for years. Many of these TACE inhibiting and other related MMP (matrix metalloproteinase) inhibiting compounds have been patented and, thus, are known. The Examiner's attention is respectfully drawn to U.S. Patent Nos. 6,326,516 B1; 6,313,123 B1; 6,225,311 B1; and 6,200,996 B1 for several examples in which an aryl (as aryl, phenyl or naphthyl) and a heteroaryl in a similar Y position are described and claimed in related structures exhibiting TACE inhibiting activity. In this series of related compounds, it is demonstrated that aryl and heteroaryl are interchangeable in the Y position without adversely affecting the integrity of the structure or the TACE inhibiting properties of the compound. With respect to these two particular substituents in the Y position, there is an art-recognized correlation between structure and function.

Despite the lack of an example where Y is a heteroaryl, Applicants had constructive possession of the elected generic compounds on the filing date of the present application. The application illustrated 125 examples of representative compounds where Y is phenyl, most of which were tested and demonstrated activity as inhibitors of the enzymes MMP-1, MMP-9, MMP-13 and/or TACE. One of ordinary skill in the art can presume, without any doubt, that the heteroaryl will readily substitute for the phenyl in all of the examples and would reasonably expect to find the TACE inhibiting activity from the heteroaryl compounds. The ordinary practitioner would understand that Applicants have possessed

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the compounds where Y is heteroaryl on the basis of numerous examples in the specification illustrating Y as phenyl and the state of the art establishing a structure-activity relationship between aryl and heteroaryl in similar compounds that work. There is no question that Applicants had possession of the compounds wherein Y is heteroaryl. Hence, the claims comply with the written description requirement.

Claims 1, 2 and 5-7 also remain rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement for reasons set forth on pages 3-5 of the Office action. Applicants respectfully traverse the rejection in light of the arguments of record (incorporated herein by reference thereto) and the following additional reasons.

Since the compounds containing Y as heteroaryl have been artificially isolated for examination purposes due to the restriction requirement, the highly exemplified phenyl compounds have been ignored. Most importantly, it should be stressed that the application is not truly devoid of all working examples. In fact, the application shows how to make and use 125 different compounds. Although there are no specific examples wherein Y is heteroaryl, the ordinary chemist would know exactly what steps to take to substitute a heteroaryl for the illustrated phenyl and successfully make the claimed compounds without undue effort. Based on the disclosure of the TACE inhibiting properties of almost 125 phenyl compounds and the structure-activity relationship shown by similar compounds in U.S. Patent Nos. 6,326,516 B1; 6,313,123 B1; 6,225,311 B1; and 6,200,996 B1, the chemist would predict the TACE inhibiting activity and appreciate how to use the claimed compounds without undue experimentation. Therefore, the application provides sufficient guidance to enable one of ordinary skill in the art to practice the claimed invention without an unexpected quantity of experimentation. Indeed, the experimentation to make and use the claimed invention would be routine.

Insofar as the breadth of the claims is concerned, the same scope as the presently recited generic claim had previously issued in the parent, granted under U.S. Patent No. 6,340,691 B1, in which the sole difference resided in Y as phenyl instead of the heteroaryl group that had been restricted out of the prior application. Due to the established correlation between phenyl and heteroaryl in the Y position of other similar, patented compounds, the exemplification of phenyl in this divisional application adequately supports the full scope of the heteroaryl compounds. Therefore, the claimed invention should not be considered extremely broad.

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With respect to Applicants' prior demonstration of the TACE inhibiting activity of two compounds from U.S. Patent No. 6,225,311, the Examiner believes that the activity of the pyridine compound is more than 4 times the activity of phenyl and concludes that the activities are very different for small differences between the structures. In reply, the Examiner's attention is respectfully drawn to the variable TACE inhibiting activities of the patented phenyl compounds shown in Table 1 on pages 111 to 114 of the present application. It will be appreciated from those values that the IC_{50} difference observed in the TACE inhibiting activity between the pyridine (29 nM) and the phenyl (7 nM) of the '311 patent is not statistically significant. Both of these compounds provide potent TACE inhibiting activity at very low dosages. Hence, the TACE inhibiting activity of the phenyl substituent will correlate to useful TACE inhibiting activity of the heteroaryl substituent in similar working compounds. In terms of enablement in the present application, the ample exemplification of phenyl compounds will support the allowance of the claims drawn to the heteroaryl compounds.

In view of the foregoing remarks, the proffered evidence and the remarks of record, Applicants respectfully ask that the Examiner withdraw the rejection of Claims 1, 2 and 5-7 under 35 U.S.C. § 112, first paragraph, and allow this application.

Favorable treatment is respectfully urged.

Respectfully submitted,

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